

WHAT IS CLAIMED IS:

1. An isolated nucleic acid encoding an osteoprotegerin binding protein selected from the group consisting of:
  - a) the nucleic acid sequence as in Figure 1 (SEQ ID NO:\_\_\_) and Figure 4 (SEQ ID NO:\_\_\_);
  - b) nucleic acids which hybridize to the polypeptide coding regions as shown in Figure 1 (SEQ ID NO:\_\_\_) and Figure 4 (SEQ ID NO:\_\_\_) and remain hybridized under high stringency conditions; and
  - c) nucleic acids which are degenerate to the nucleic acids of (a) or (b).
2. The nucleic acid of Claim 1 which is cDNA, genomic DNA, synthetic DNA or RNA.
3. A polypeptide encoded by the nucleic acid of Claim 1.
4. The nucleic acid of Claim 1 including one or more codons preferred for Escherichia coli expression.
5. The nucleic acid of Claim 1 having a detectable label attached thereto.
6. A nucleic acid encoding a polypeptide comprising the amino acid sequence of residues 1-316 and residues 70-316 as shown in Figure 1 (SEQ ID NO: \_\_\_).
7. A nucleic acid encoding a polypeptide comprising amino acid sequence of residues 1-317 and residues 69-317 as shown in Figure 4 (SEQ ID NO:\_\_\_);

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8. A nucleic acid encoding a soluble osteoprotegerin binding protein.

9. The nucleic acid of Claim 8 encoding a polypeptide comprising residues 69-317 as shown in Figure 4 (SEQ ID NO:\_\_\_) and truncations thereof;

10. An expression vector comprising the nucleic acid of Claims 1 and 9.

11. The expression vector of Claim 10 wherein the nucleic acid comprises the polypeptide-encoding region as shown in Figure 1 (SEQ ID NO:\_\_\_) and Figure 4 (SEQ ID NO:\_\_\_);

12. A host cell transformed or transfected with the expression vector of Claim 10.

13. The host cell of Claim 12 which is a eucaryotic or procaryotic cell.

14. The host cell of Claim 13 which is Escherichia coli.

15. A process for the production of an osteoprotegerin binding protein comprising:  
growing under suitable nutrient conditions host cells transformed or transfected with the nucleic acid of Claim 1; and  
isolating the polypeptide product of the expression of the nucleic acid.

16. A polypeptide produced by the process of Claim 15.

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17. A purified and isolated osteoprotegerin binding protein, or fragment, analog, or derivative thereof.

5 18. The protein of Claim 17 which is a human osteoprotegerin.

10 19. The protein of Claim 17 having the amino acid sequence as shown in Figure 1 (SEQ ID NO:\_\_\_) and Figure 4 (SEQ ID NO:\_\_\_).

20. The protein of Claim 17 which has been covalently modified with a water-soluble polymer.

15 21. The protein of Claim 20 wherein the polymer is polyethylene glycol.

20 22. The protein of Claim 17 which is a soluble osteoprotegerin binding protein.

25 23. The protein of Claim 22 comprising the amino acid sequence from residues 70-316 inclusive as shown in Figure 1 (SEQ ID NO: \_\_\_), or a fragment, analog, or derivative thereof.

30 24. The protein of Claim 22 comprising the amino acid sequence from residues 69-317 inclusive as shown in Figure 4 (SEQ ID NO:\_\_\_) and truncations thereof.

25. An antibody or fragment thereof which specifically binds an osteoprotegerin binding protein.

35 26. The antibody of Claim 25 which is a monoclonal antibody.

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27. A method for detecting the presence of an osteoprotegerin binding protein in a biological sample comprising:

5           incubating the sample with the antibody of Claim 25 under conditions that allow binding of the antibody to the osteoprotegerin binding protein; and detecting the bound antibody.

10           28. A method for detecting the presence of osteoprotegerin in a biological sample comprising:

          incubating the sample with an osteoprotegerin binding protein under conditions that allow binding of the protein to osteoprotegerin; and  
15           measuring the bound osteoprotegerin binding protein.

29. A method to assess the ability of a candidate compound to bind to an osteoprotegerin binding protein comprising:

20           incubating the osteoprotegerin binding protein with the candidate compound under conditions that allow binding; and measuring the bound compound.

25           30. The method of Claim 29 wherein the compound is an agonist or an antagonist of an osteoprotegerin binding protein.

30           (31). A method of regulating expression of an osteoprotegerin binding protein in an animal comprising administering to the animal a nucleic acid complementary to the nucleic acids as shown in Figure 1 (SEQ ID NO:\_\_\_) and Figure 4 (SEQ ID NO: \_\_\_).

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32. A pharmaceutical composition comprising a therapeutically effective amount of an osteoprotegerin binding protein in a pharmaceutically acceptable carrier, adjuvant, solubilizer, stabilizer and/or anti-oxidant.

33. The composition of Claim 32 wherein the osteoprotegerin binding protein is a human osteoprotegerin binding protein.

34. A method of treating bone disease in a mammal comprising administering a therapeutically effective amount of a modulator of an osteoprotegerin binding protein.

35. The method of Claim 34 wherein the modulator is a soluble form of an osteoprotegerin binding protein.

36. The method of Claim 35 wherein the modulator is an antibody, or fragment thereof, which specifically binds an osteoprotegerin binding protein.

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